REMARKS

The presently claimed invention related to probes that include a region that incorporates at least one nucleotide label and at least one inosine residue and that does not hybridize to the target under specified high stringency conditions. As the specification explains, probes of this type are useful, in part, because they can exhibit reduced non-specific target binding compared to probes that do not include inosine residues (see Examples).

Rejections Under 35 U.S.C. §103

The Examiner rejected claim 1 as obvious in view of O'Neil et al. (U.S. Patent No. 6,124,092) taken with Byng et al. (U.S. Patent No. 4,917,999). According to the Examiner, O'Neil et al. describes primers having a portion that does not hybridize to the target and is used as a "recovery tag" that can hybridize to its complement thereby facilitating isolation of elongated primers. According to the Examiner, Byng et al. discloses probes that include multiple inosine residues and various labels. The Examiner concludes that it would have been obvious to modify "the probe/primer of O'Neil et al. such that it comprised inosinic residues as disclosed by Byng et al. as such would have afforded the artisan the ability to readily and reproducibly detect similar or related sequences with having to resort to the time, labor and expense of manufacturing additional probes."

Applicants respectfully traverse this rejection.

The probes of claim 1 includes a region "having a sequence comprising .. . at least one inosinic acid or derivative thereof" and certain labeled nucleotides. This region is incapable of "hybridizing under stringent conditions to any nucleotide sequence of the target nucleotide sequence, wherein said stringent conditions are 6 x SSC, 0.5% sodium dodecyl sulfate, and 5 x Denhardt's reagent, pH is 7.0 at 68°C". Thus, the portion of the claimed probes which does not hybridize under stringent conditions to the target contains inosine residues.

The Examiner appears to be suggesting that the presently claimed probes are obvious because it would have been obvious to modify the primer of O'Neil et al. to include inosine residues into the recovery tag portion of the primer. In fact, not only would the teachings of

O'Neil et al. and Byng et al. not lead to such a modification of the primer described by O'Neil, but would actually suggest that such a modification not be made. O'Neil et al.'s primers include a recovery tag so the several different primers can be combined in a single sequencing reaction, for example, to sequence different portions of the same target molecule. In order to interpret the sequences the extension products of each of the different primers must be isolated. O'Neil et al. achieves this isolation by having the recovery tag of each primer be unique to the primer. This allows each recovery tag to selectively bind to its complementary sequence so that each primer can be isolated from the other primers and analyzed separately (see Figure 1 of O'Neil et al.). Thus, the method relies on highly specific hybridization of each recovery tag to its complementary sequence.

Inosine residues base-pair in a relatively non-selective manner. This is very reason that Byng et al. incorporates inosine residues into probes at positions where the sequence of the complement (target) is unknown or uncertain. Thus, were one to introduce inosine residues into the recovery tag portion of the primer of O'Neil et al., the recovery tag would be less specific for hybridization to its complementary sequence and it would become more difficult to isolate each of the different primers. The ability to isolate different primers that have been combined in a single sequencing reaction is the goal of the methods described by O'Neil et al. Thus, far from encouraging the modification of the recovery tags of O'Neil et al. to include inosine residues, the cited references suggest to one skilled in the art that such a modification should not be made. Accordingly, the cited references amount to teaching away from the modification suggested by the Examiner. As the Court of Appeals for the Federal Circuit has explained "We have noted ... as a 'useful general rule,' that references that teach away cannot serve to create a prima facie case of obviousness." *McGinley v. Franklin Sports, Inc.*, 262 F.3d 1339 (Fed. Cir. 2000). Thus, the cited references cannot render claim1 obvious. In view of forgoing, Applicants respectfully request that this rejection under 35 U.S.C. §103 be withdrawn.

Rejections Under 35 U.S.C. §102

The Examiner rejected claim 11 as anticipated by GIBCO BRL Products & Research Guide ("GIBCO/BRL Catalog"), a catalog of products useful in biochemistry and molecular biology. The Examiner argued that claim 11 is anticipated because the various components of the claimed kit are offered for sale in the catalog.

Applicants respectfully traverse this rejection.

While the GIBCO/BRL Catalog describes, among the hundreds of products offered, terminal transferase and various labeled and unlabeled nucleotides, it does not discloses terminal transfer and the nucleotides specified by claim 11 together in a kit, as required by claim 11. In view of this, the GIBCO/BRL Catalog cannot anticipate the kit of claim 11.

In view of the forgoing, Applicants respectfully request that this rejection under 35 U.S.C. §102(b) be withdrawn.

Enclosed is a Petition for Extension of Time with the appropriate fee. Please apply any other charges or credits to deposit account 06-1050.

Respectfully submitted,

Date: 20 MARCH 2006

Anita L. Meiklejohn, Ph.D.
Reg. No. 35,283

Fish & Richardson P.C.
225 Franklin Street
Boston, MA 02110
Telephone: (617) 542-5070
Facsimile: (617) 542-8906